SUMMARY OF THE REJECTIONS

Claims 3 and 13-15 have been rejected under 35 USC 112, second paragraph

The basis for this rejection is the assertion that the terms "the medical device" and "said medical device" do not find "sufficient antecedent basis" in claim 1.

Claims 1, 2, 10, 11 and 17 have been rejected under 35 USC 102(b) as anticipated by Judd et al. (U.S. Patent No. 5,910,112)

It is asserted that Judd et al. teach each and every limitation of these claims by the teaching of an MRI device for observing viability of heart cells, which could have come from a transplanted heart, comprising non-destructive monitoring of Na-23 levels (citing particularly column 3, lines 10-30).

Claims 1-4 have been rejected under 35 USC 102(b) as anticipated by Lemelson (U.S. Patent No. 5,571,083)

It is asserted that Lemelson teaches a method and system for cell transplantation, comprising the use of an MRI imager to guide and position a medical device (column 2, lines 30-67).

Claims 1, 2, 5-9, 12-16 and 23-29 have been rejected under 35 USC 103(a) as unpatentable over Wald et al. (U.S. Patent No. 6,181,134) and Aebischer et al. (U.S. Patent No. 5,487,739)

This rejection asserts that claims 1, 2, 5-9, 12-16 and 23-29 are taught by the disclosure of Wald showing an MRI imager for determining cell viability using an RF coil (column 4, line 25) by cell activity determination of lactate level (column 4, lines 60-65), as well as local concentration of NAA, choline and creatine (column 5, lines 5-16). However, the reference does not teach the use of imaging systems to visualize transplanted cells. Aebisher et al. is asserted to teach the use of an MRI system to monitor a transplanted cell (column 5, line 15). It is therefore asserted to be obvious to adapt the teachings of Aebischer et al. to Wald's device such that the use of the imager could be extended to post-transplanted observation of cell viability.

Claims 1, 2 and 18-22 are rejected under 35 USC 103(a) as unpatentable over Rockledge et al. (Rocklage et al., U.S. Patent No. 5,833,947) **[apparently in view of Aebisher, *supra*,]**

This rejection asserts that Rocklage et al. teaches an MRI imager for determining cell viability by observing blood flow change and infusion of T1 shortening agent to increase the contrast of T2 agent (Column 11, lines 15-20). However, there is no teaching of the use of the imager to view transplanted cells. Aebischer, however, teaches the use of an MRI imager to monitor transplanted cells (Column 5, line 15). It is asserted to be obvious to "adapt the teachings of Aebischer to Rochlage's device such that the use of the imager could be extended to post-transplanted observation viability."

RESPONSE TO THE REJECTIONS

The Rejections Under 35 USC 112, second paragraph

These rejections have been overcome by the above amendments to the claims. It is to be noted, however, that claim 1 clearly contains the limitation of "a medical device" so that reference in later claims to "said medical device" or "the medical device" is correct.

INTRODUCTION TO THE TRAVERSAL OF ALL REJECTIONS BASED ON PRIOR ART UNDER 35 USC 102(b) OR 35 USC 103(a)

It is to be noted that the present invention is directed towards implantation of cells, not organs or tissues. This has been clarified by amendments to the claims to emphasize the differences, and not to alter the essential direction of the invention as claimed. This is an important consideration as the prior art deals exclusively with the macro-techniques of organ transplantation and evaluation of organ viability. The present invention deals with micro-techniques of cell implantation and the assessment of cell viability . New claims indicate that implantation of a colony of cells (clearly distinguishing from transplantation of an organ) clarifies that the invention is normally practiced using an implant, usually considered to be in the range of between 100 and 10,000,000 cells. However, this is much more than a mere differentiation in size or number of cells, but is a fundamental difference in technology. The difference may be analogized as evaluating organ transplantation being similar to detecting a metal airplane

in flight, while evaluating cell implantation viability is comparable to determination of parts per billion concentrations of metal in an environment. Even though a generic objective (e.g., metal detection) is performed in both events, the methodology, programs, and even equipment is vastly different. This underlying difference, clearly expressed in amended claims 1 and 27 (from which all of claims 2-26 and 29 depend) and in new claims 30-32, must be considered in evaluation the substantial differences between the prior art and the claimed invention.

Rejection of Claims 1, 2, 10, 11 and 17 Over Judd et al. (US Patent 5,910,112) Under 35 USC 102(b)

This rejection must basically fail for the reasons expressed above to be generally considered in all issues of the prior art of record. The Judd et al. reference shows a method for improved MRI efficiency in determining, for example, ^{23}Na concentrations in heart tissue to determine the viability of tissue in the heart. The Rejection then asserts that it is now obvious to both transplant hearts (e.g., asserting that a heart transplant is equivalent to cell implantation) and to check for tissue viability with regard to the transplanted heart. By equating organ transplants to cell implantation therapy, the rejection asserts anticipation.

This rejection is less than sufficient to show anticipation of our invention. Even the original recitation of "transplanted cells" distinguished from transplantation of organs. The new language reciting cell implantation of:

"implanted stem cells, progenitor cells, or differentiated cells"

clearly differentiates the language of the claimed invention from the teachings of Judd et al. These claims now emphasize cell implantation as opposed to organ transplantation. Cells used for cell implants are anatomically, biochemically, and physiologically distinguishable from entire organs used in organ transplants. As Judd et al. do not teach implanting cells, and as the macro-technology of Judd et al. is not the same as the micro-technology of the claims where cell implanting is performed, the rejection under 35 USC 102(b) is clearly in error.

It is to be further noted that Judd et al. shows viewing of the imaging at about fifteen minutes after initial data is generated (e.g., column 2, lines 54-63). There are new

limitations in new claims (for which proper antecedent basis is clearly denoted) reciting viewing of an image from sensing in less than five minutes or in near real time. These claims also further recite limitations that are not obvious from Judd et al.

The limitations of claims 41-47 showing quantitating of cell viability is also not suggested by Judd et al., either with or without the faster response rate of viewing images for sensing of the implanted cells.

Rejection of Claims 1-4 Over Lemelson (US Patent 5,571,083) Under 35 USC 102(b)

This rejection is weaker that the rejection over Judd et al. Although Lemelson is effective in showing the use of "visualization techniques with MRI," the process essentially visualizes the equipment, visualizes the location of tissues into which cells are to be transplanted, but not to biochemical changes underlying cell metabolic viability and physiologic function. There is no disclosure in Lemelson for viewing the sensing of data relating to survivability of cells. The only reference to "survivability" of cells is immediately before the examples wherein it is suggested that cells do not survive well (Column 9, lines 45-55). This reference is not relevant to the claimed invention. The rejection under 35 USC 102(b) is clearly in error, and any attempt to modify the rejection to consideration of issues under 35 USC 103(a) is also clearly in error.

Rejection of Claims 1, 2, 5-9, 12-16 and 23-29 Under 35 USC 103(a) Over Wald (US Patent No. 6,181,134) in view of Aebischer et al. (US Patent 5,487,739)

The value of the teachings of the references has again been overvalued with regard to anticipation or suggestion of actual limitations in the claims. For example, the rejection asserts that on column 4, lines 60-65 of Wald is taught a process of 'cell activity determination' by observing chemical levels. Review of that section of the text gives only the most inferential indication of cell activity, and that of a different nature than our practice. Specifically, continuing that passage onto column 5 there is an indication that chemical analysis through MR imaging can indicate cancer. This is not clearly a direct indication of cell activity but rather events or the existence of an abnormal class of cells. There is no teaching that the normal condition or metabolic fluctuations of benign cells

can be specifically determined, and that the viability of implanted cultured cells can be determined by an MRI methodology.

The citation of Aebischer is even less effective for teaching the issues of the the present invention. That reference is cited (Column 5, line 15) as teaching the visualization for transplanted cells. All that is done is visual analysis using dyes in conventional gross tissue observation. The presence of dyes differentially absorbed by different classes of tissues would not in any way teach the use of MRI imaging to determine cell viability. At most, the presence of the transplanted cells could be visualized, but no determination of immediate viability could be established. If dyes were used in this manner on the dyes before implantation, the dyes would remain with the cells after transplant, whether the cells were viable or not.

Rejection of Claims 1, 2, and 18-20 Under 35 USC 103(a) Over Rocklage and Kucharczyk (US Patent 5,190,744)

This rejection also fails to be instructive of even the original language of the claims. The Rocklage reference teaches looking for blood flow anomalies, and does not directly or indirectly deal with determining cell implant viability. Although not cited in the rejection, Aebischer et al. is again used to assert the obviousness of cell transplantation (although, as noted above, that reference merely teaches gross cell observation through enhanced imaging with dye injection). It is not apparent how one of ordinary skill in the art can comprehend how blood "flow" analysis can be equated with chemical analysis/identification by MRI to assert obviousness. These are substantively different objectives effected by substantively different process steps that are recited in the claims in this Application.

Applicants assume the application is now in proper order and in condition for examination. Please direct any inquiries to the undersigned attorney at (952) 832-9090.

Respectfully submitted,

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CERTIFICATE UNDER 37 C.F.R. 1.8: The undersigned hereby certifies that this Transmittal Letter and the paper, as described herein, are being deposited in the United States Postal Service, as first class mail, with sufficient postage, in an envelope addressed to: Assistant Commissioner for Patents, Box Amendment, Washington, D.C. 20231 on February 4, 2002.

Mark A. Litman
Name

_____
Signature